

***Remarks***

Reconsideration of this Application is respectfully requested.

The foregoing amendments to the claims are believed to place the claims into condition for immediate allowance or into better condition for consideration on appeal. It is respectfully believed that these amendments do not raise new issues that would require an additional search. Entry of the amendments after final rejection is respectfully requested.

No new matter is added to the present application by the foregoing amendments, which are fully supported in the specification as originally filed. Upon entry of the foregoing amendment, claims 47-63 and 106-116 are pending in the application, with claim 47 being the independent claim. Support for the amendment to claim 47 can be found on page 7 of the specification. Support for the amendment to claim 50 and for new claims 108-110 can be found on page 7 of the specification. Support for new claims 111-113 can be found on pages 21-22 of the specification. Support for claim 114 can be found on page 23 of the specification. Support for claims 115-116 can be found on page 20 of the specification.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejections under 35 U.S.C. § 112, first paragraph***

In the Office Action, at page 2, section 2, claims 47-63 and 106-107 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically,

the Examiner stated that claim 47 "is indefinite with respect to the phrase 'one or more cDNA molecules or a population of cDNA molecules'." Applicants respectfully traverse this rejection and reiterate herein their arguments set forth in the Amendment and Reply filed on May 13, 2003. Solely in an effort to expedite prosecution, and without acquiescing with the propriety of the rejection, however, Applicants have amended claim 47 to delete "a population of cDNA molecules" from the claims. Withdrawal of the rejection is respectfully requested.

In the Office Action, at page 3, section 4, claims 47, 52 and 53 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite "with respect to the differences between 'reduce or substantially reduce.'" Applicants respectfully traverse this rejection and reiterate herein their arguments set forth in the Amendment and Reply filed on May 13, 2003. Solely in an effort to expedite prosecution, and without acquiescing with the propriety of the rejection, however, Applicants have amended claims 47, 52 and 53 to delete the term "substantially reduce" from the claims. Withdrawal of the rejection is respectfully requested.

In the Office Action, at page 3, section 8, claim 50 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite because the term "low" "is a relative term that renders the claim indefinite." Applicants respectfully traverse this rejection and reiterate herein their arguments set forth in the Amendment and Reply filed on May 13, 2003. Solely in an effort to expedite prosecution, and without acquiescing with the propriety of the rejection, however, Applicants have amended claim 50 to specify a temperature below about 90°C. Withdrawal of the rejection is respectfully requested.

***Rejections under 35 U.S.C. § 103(a)***

In the Office Action, at page 5, section 14, claims 47-63 and 106-107 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Scalice *et al.* (U.S. Patent No. 5,338,671) in view of Myers *et al.* ("Reverse transcription and DNA Amplification by a *Thermus Thermophilus* DNA Polymerase," *Biochemistry* 30:7661-7666 (1991)), Clontech (96/97 Catalog No. 5400-1 and 5400-2, p. 41 (1996)) and Odawara (U.S. Patent No. 5,989,819). Applicants respectfully traverse this rejection and reiterate herein their arguments set forth in the Amendment and Reply filed on May 13, 2003.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). There is no basis for concluding that an invention would have been obvious solely because it is a combination of elements that were known in the art at the time the invention was made. *See Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556 (Fed. Cir. 1995). Instead, what is needed is a reason, suggestion, or motivation in the prior art that would motivate one of ordinary skill to combine the cited references, and that would also suggest a reasonable likelihood of success in making or using the claimed invention as a result of that combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). In the present case, this burden has not been satisfied.

The claimed methods involve the inhibition, prevention or reduction of non-specific cDNA products produced during *reverse transcription*; such conditions may include the use

of reverse transcriptase inhibitors, such as reverse transcriptase-specific antibodies. Thus, Applicants are confused by the statement at page 6, section 16, of the Office Action:

For purposes of examination, the claims have been interpreted as encompassing the production of cDNA molecules from either RNA or from prior cDNA through an amplification reaction such as PCR.

Applicants respectfully draw the Examiner's attention to the language of claim 47, in which the template for cDNA synthesis is unambiguously identified as either mRNA or poly A RNA. Thus, the claims clearly do not encompass the production of cDNA molecules from prior cDNA through an amplification reaction such as PCR. The Examiner's interpretation of the claims is not accurate.

The Scalice reference is not relevant to the claimed invention, because Scalice does not teach methods for inhibiting, preventing or reducing non-specific cDNA products produced during *reverse transcription*. Instead, Scalice teaches that "It would be desirable to reduce or eliminate the formation of nonspecific products and primer dimers *in PCR*." Scalice at col. 2. Indeed, none of the methods described in Scalice relate to reverse transcription at all. Thus, Scalice does not disclose, suggest, or otherwise contemplate the invention as claimed. Hence, Scalice is seriously deficient as a primary reference in the attempt to establish a *prima facie* case of obviousness.

At page 8, section 27, of the Office Action, the Examiner states that it would have been obvious to modify the method of Scalice with that of Myers, whereby the cDNA is synthesized with the *Tth* polymerase under conditions where the polymerase exhibits reverse transcriptase activity, because Myers teaches that the *Tth* polymerase is also an efficient reverse transcriptase. The Examiner further states that the ordinary artisan would have been

motivated to have employed inhibitory anti-*Tth* antibodies as disclosed by Scalice because they have been shown to reduce non-specific priming. Applicants respectfully disagree.

The Examiner's statement in section 27 appears to misapprehend where the required motivation must arise in order for a *prima facie* case of obviousness to be established. Applicants respectfully remind the Examiner that the requisite motivation for establishing a *prima facie* case of obviousness *must* be found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *See In re Kotzhab*, 217 F.3d 1365 (Fed. Cir. 2000). Moreover, the mere fact that an advantage *might* be realized by combining reference teachings does not mean that a skilled artisan would be motivated to do so. *See In re Mills*, 916 F.2d. 680, 682 (Fed. Cir. 1992) (Although a prior art device "may be capable of being modified to run the way the apparatus is claimed, there must be a suggestion or motivation in the reference to do so.")

The cited art (including Scalice) is silent about the use of conditions that inhibit the formation of non-specific cDNA products during *reverse transcription*. There is absolutely *nothing* in Scalice or any of the other cited references concerning the problem of non-specific product generation during reverse transcription reactions or how one might solve such a problem. Thus, the cited references would not have motivated one of ordinary skill in the art to achieve the present invention.

As discussed above, Scalice teaches antibodies for use *during PCR* and does not disclose, suggest, or otherwise contemplate the invention as claimed. Scalice mentions that DNA and RNA starting materials present in a sample can be detected, and provides a solution for the detection problem presented by the formation of non-specific products *during PCR*. Scalice never recognizes, much less purports to solve, the problem of reducing non-specific products during *reverse transcription*. Although Myers teaches that *Tth* polymerase

Scalice never recognizes, much less purports to solve, the problem of reducing non-specific products during *reverse transcription*. Although Myers teaches that *Tth* polymerase possesses reverse transcriptase activity, Myers also does not disclose, suggest or otherwise contemplate the use of a reverse transcriptase inhibitor to reduce the formation of non-specific products. Therefore, neither reference provides the requisite suggestion or motivation to practice the claimed invention. Moreover, neither reference provides the requisite suggestion or motivation to combine their teachings, nor a suggestion that the outcome of such a combination would result in the claimed invention. Thus, the cited references, alone or in combination, fail to establish a *prima facie* case of obviousness.

The Examiner further cites the teachings in Odawara, who discloses anti-reverse transcriptase antibodies. Odawara teaches a method for quantitatively determining the presence of an antibody capable of inhibiting reverse transcriptase activity. Although Odawara discloses such antibodies, Odawara does not disclose or suggest using them in the methods claimed in the present invention, nor does Odawara suggest that such antibodies could be useful inhibitors of the synthesis of non-specific cDNA products. Thus, again, Odawara is seriously deficient as a reference and lacks the requisite motivation to combine its teachings with Scalice or Myers.

It appears that the Examiner is attempting to find the required motivation to combine the cited references in Applicants' own specification rather than in the cited art. As the Federal Circuit has held numerous times, however, such a hindsight analysis is impermissible. Instead, the Examiner must show suggestions, explicit or otherwise, that would compel one of ordinary skill to combine the cited references in order to make and use the claimed invention. Thus, because the Examiner has provided no actual evidence to

Applicants also note that at pages 9-10, sections 31-32, of the Office Action, it appears that the Examiner is making the argument that the present invention is inherently obvious in view of the cited references: "[t]o the extent that the polypeptide is used under conditions whereby it exhibits reverse transcriptase activity, Scalice *et al.*, clearly teach that their antibodies bind to said protein, and Odawara also teaches the production of antibodies that bind to not just any reverse transcriptase, but to those that are of viral origin."

The law is clear that there is no inherent obviousness. It is a well-established principle of law that "[t]hat which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *In re Spormann*, 363 F.2d 444, 448. "Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection." *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993); *See also In re Newell*, 891 F.2d 889, 901 (Fed. Cir. 1989).

Finally, Applicants have amended claim 47 to make explicit that which is implicit in the claim, by adding the phrase "wherein said inhibitor inhibits said reverse transcriptase activity under said conditions." This amendment addresses the Examiner's concern at page 9, section 31, of the Office Action regarding the lack of requirement that the inhibitor actually inhibit reverse transcriptase activity. Applicants respectfully request that the rejection of claims 47-63 and 106-107 under 35 U.S.C. § 103(a) be withdrawn.

### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the

outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: May 21, 2004

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